UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
[illegible]	[illegible]	[illegible]	[illegible]

WO[illegible] WASHBURN KURTZ
MA[illegible] & NORRIS
ONE LIBERTY PLACE 4 TH FLOOR
PHILADEPHIA PA 1910[illegible]

EXAMINER	
[illegible]	
ART UNIT	**PAPER NUMBER**
[illegible]	11

DATE MAILED: 10/[illegible]

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev 11/00)

1- File Copy

Office Action Summary	Application No.	Applicant(s)	
	09/485,421	MAHALINGAM ET AL.	
	Examiner	Art Unit	
	Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *12-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 October 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *5*
4)☐ Interview Summary (PTO-413) Paper No(s). _____
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other.

DETAILED ACTION

The amendment filed on July 20, 2001 has been entered as Paper #7. The Examiner assigned to your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to examiner Q. Janice Li, at Group Art Unit 1632.

Claims 1-27 are pending in the application.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-11, in Paper No. 7 is acknowledged. The traversal is on the ground(s) that the Examiner has not shown separate classification, status in the art or a requirement for a different field of search, accordingly, all pending claims should be examined in the present application without restriction. In response, the claims were restricted under 371 practice, US classification does not apply.

The invention listed as groups I-IV do not relate to a single inventive concept under PCT Rule 13.1, because under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Groups I-III are drawn to different products, namely, a DNA-protein conjugates, a protein, and a nucleic acid, and different methods of using such molecules. The different products belong to distinct chemical entities, therefore, each acquires distinct status in the art. Groups I-IV are further drawn to different methods. These methods have different inventive steps,

different mode of operation, generate different products, and/or use different starting materials. 37 CFR 1.475 (b) states "AN INTERNATIONAL OR A NATIONAL STAGE APPLICATION CONTAINING CLAIMS TO DIFFERENT CATEGORIES OF INVENTION WILL BE CONSIDERED TO HAVE UNITY OF INVENTION IF THE CLAIMS ARE DRAWN **ONLY TO ONE** OF THE FOLLOWING COMBINATIONS OF CATEGORIES: (1) A PRODUCT AND A PROCESS SPECIALLY ADAPTED FOR THE MANUFACTURE OF SAID PRODUCT; OR (2) A PRODUCT AND A PROCESS OF USE OF SAID PRODUCT;OR (3) A PRODUCT, A PROCESS SPECIALLY ADAPTED FOR THE MANUFACTURE OF THE SAID PRODUCT, AND A USE OF THE SAID PRODUCT; OR (4) A PROCESS AND AN APPARATUS OR MEANS SPECIFICALLY DESIGNED FOR CARRYING OUT THE SAID PROCESS; OR (5) A PRODUCT, A PROCESS SPECIALLY ADAPTED FOR THE MANUFACTURE OF THE SAID PRODUCT, AND AN APPARATUS OR MEANS SPECIFICALLY DESIGNED FOR CARRYING OUT THE SAID PROCESS." Since multiple products and multiple processes of using are claimed, unity of invention is lacking and restriction is proper. The differences in the special technical features of the Inventions I-IV are further underscored by their divergent classification and independent search criteria.

Furthermore, as cited in the International Preliminary Examination Report, Group I is anticipated or obvious over the cited prior art of record (WO96/08970). Applicants are advised to see 37 CFR 1.475 (a)-(d) for details. 37 CFR 1.475 (a) recites "AN INTERNATIONAL AND A NATIONAL STAGE APPLICATION SHALL RELATED TO ONE INVENTION ONLY OR TO A GROUP OF INVENTIONS SO LINKED AS TO FORM A SINGLE GENERAL INVENTIVE CONCEPT ('REQUIREMENT OF UNITY OF INVENTION'). WHERE A GROUP OF INVENTIONS IS CLAIMED IN AN APPLICATION, THE REQUIREMENT OF UNITY OF INVENTION SHALL BE FULFILLED ONLY WHEN THERE IS A TECHNICAL RELATIONSHIP AMONG THOSE INVENTIONS INVOLVING ONE OR MORE OF THE SAME OR CORRESPONDING SPECIAL TECHNICAL FEATURES." The expression "special technical features"

shall mean those technical features that define a contribution, which **each** of the claimed inventions, considered **as a whole**, makes over the prior art. Because WO96/08970 is obvious over group I, the special technical feature of group I does not provide a contribution over the prior art as a whole with groups II-IV, so unity of invention is lacking.

Therefore, it is maintained that these inventions are distinct due to their divergent subject matter and are thus, separately classified and searched. The requirement is deemed proper and is therefore made **FINAL**.

Please note that after a final requirement for restriction, the Applicants, in addition to making any response due on the remainder of the action, may petition the Commissioner to review the requirement. Petition may be deferred until after final action on or allowance of claims to the invention elected, but must be filed not later than appeal. A petition will not be considered if reconsideration of the requirement was not requested. (See § 1.181.).

Claims 1-27 are pending, however, claims 12-27 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions. Claims 1-11 are under current examination.

Specification

The specification contains sequence disclosures (Figures 5) that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2) but are not present in the Sequence Listing and/or

identified in the specification by sequence identifier numbers. Applicant must provide a paper copy and a computer readable copy of the Sequence Listing and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). A full response to this Office Action must include a complete response to the requirement for a Sequence Listing.

Claim Objections

Claim 1 is objected to because of the following informalities: "amino acids" in line 2 is recited twice. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims recite " a non-HIV-1 vpr protein", the specification teaches "non-vpr protein is meant to refer to a protein that is not identical to HIV-1 Vpr protein. The term 'non-Vpr protein which has a sequence of a fragment of Vpr protein' is meant to refer to

a non-Vpr protein which has an amino acid sequence identical in part to that of a fragment of Vpr protein and additional amino acid residues which differ from those of Vpr protein...". In view of the breadth of the claims, they embrace a genus of the proteins protein which has an amino acid sequence identical in part to that of a fragment of Vpr protein and additional amino acid residues which differ from those of Vpr protein...". However, neither the sequence, the chemical and physiological characteristics of the protein, nor structure-function relationships of the genus of proteins are disclosed in the specification. The specification fails to disclose *any protein* that would be identified as a "non-Vpr protein which has a sequence of a fragment of Vpr protein". The claimed invention has not been set forth in terms of distinguishing characteristics as evidenced by other descriptions of the invention. Therefore, the specification does not provide an adequate written description of the claimed invention in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant is referred to the Revised Interim Guidelines for "Written Description" requirement published December 21, 1999 in the Federal Register, Volume 64, Number 244, pages 71427-71440. "Possession may be shown in any number of ways. Possession may be shown by actual reduction to practice, by a clear depiction of the invention in detailed drawings...or by a written description of the invention describing sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention." (page 71435, middle column, first paragraph of "a") The skilled artisan cannot envision the detailed chemical structure of all of the encompassed molecules, and therefore conception is not achieved until reduction to

practice has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 5-11 are rejected under 35 U.S.C. 102(b) as being anticipated by *WO9608970*.

These claims are directed to a conjugated composition comprising a fragment of either HIV-1 Vpr or a non HIV-1 Vpr protein comprising the amino acid sequences 17-36

or 59-84 conjugated to a therapeutic compound, wherein the compound is a DNA vaccine plasmid, wherein the compound is an antisense molecule or oligonucleotide. Claims 7-11 are further drawn to a method of delivering said composition to the nucleus of a cell.

WO9608970 teaches a composition comprising a vpr protein or a fragment thereof, conjugated to nucleic acid molecules, and such conjugated molecule could be efficiently transported into the cell nucleus, wherein the preferred embodiment of the nucleic acid molecule is an expression vector or an antisense molecule (see paragraph bridging pages 36 &37). The vpr protein taught by *WO9608970* comprises amino acid residues 59-84 or 17-36, thus, *WO9608970* anticipates the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over *WO9608970* as applied to claims 1, 3, 5-11 above, and further in view of *Katz et al* (US 6,005,004) or *Kayyem et al* (US 6,232,295).

These claims are drawn to a conjugated vpr-nucleic acid composition further comprising a *polycationic amino acid sequence* conjugated with the composition by ionic bonds. *WO9608970* fails to teach such a polycationic amino acid sequence.

However, *Katz et al* teach to selectively transport therapeutic material to brain cells using lipophilic-polycationic delivery systems comprising a biologically active molecule covalently bonded with cationic carriers and permeabilizer peptides to overcome the difficulty and enhance efficiency for drug delivery to neuronal cells (see abstract). They go on to teach such biologically active molecules comprise polypeptides, nucleic acids, oligonucleotides and transfection vectors (see claims 1-5). *Kayyem et al* teach a gene delivery system comprises polymeric molecule complexed with a nucleic acid vector and attached to at least one cell targeting moiety and using such for intracellular delivery (claims 1&2), Kayyem et al teach that such polymeric molecule will improve the current liposome system for cell specific genetic material delivery (Column 2, paragraphs 4-6).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods of *WO9608970*, by simply adding a polycationic peptide sequence to the vpr conjugated composition to further enhance intracellular delivery of nucleic acids as taught by *Katz et al* or *Kayyem et al*. The ordinary skilled artisan would have been motivated to do so for efficient intracellular drug delivery with a reasonable expectation of success. Thus, the claimed invention as a whole was clearly *prima facie* obvious in the absence of evidence to the contrary.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen M Hauda can be reached on 703-305-6608. The fax numbers for the organization where this application or proceeding is assigned are 703-308-8724 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Kay Pinsky, whose telephone number is (703) 305-3553.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).

Q. Janice Li
Examiner
Art Unit 1632

QJL
October 22, 2001

ROBERT A. SCHWARTZMAN
PRIMARY EXAMINER